

CLAIMS:

1. An *in vitro* method for diagnosing or detecting a predisposition to a disease or disorder associated with abnormal Vascular Endothelial Growth Factor gene expression, the method comprising examining a region around 405 bases 3' of the transcription start of the Vascular Endothelial Growth Factor gene or examining a region around 460 bases 5' of the transcription start of the Vascular Endothelial Growth Factor gene to detect the presence of a genetic polymorphism which is linked to the disease or disorder.
2. A method as claimed in claim 1 carried out on genomic DNA.
3. A method as claimed in claim 2 in which the genomic DNA is isolated from blood or tissue samples.
4. A method as claimed in any preceding claim 4 wherein which region around 405 bases 3' of the transcription start of the Vascular Endothelial Growth Factor gene is examined to detect the presence of a genetic polymorphism from Guanine to Cytosine.
5. A method as claimed in any one of claims 1 to 3 wherein which region around 460 bases 5' of the transcription start of the Vascular Endothelial Growth Factor gene is examined to detect the presence of a genetic polymorphism from Cytosine to Thymine.
6. A method as claimed in any preceding claims wherein the presence of a genetic polymorphism is determined by amplification of at least a fragment of the DNA by polymerase chain reaction (PCR).

7. A method as claimed in claim 6 in which the DNA is subjected to PCR amplification using PCR primers specific for the region defined by claim 4.
8. A method according to claim 7 wherein the primers are:
5'ATTTATTTTGCTTGCCATT3' (SEQ ID No. 1); and
5'GTCTGTCTGTCTGTCCGTCA3' (SEQ ID No. 2)
9. A method as claimed in claim 6 in which the DNA is subjected to PCR amplification using PCR primers specific for the region defined by claim 5.
10. A method according to claim 9 wherein the primers are:
5'TGTGCGTGTGGGGTTGAGCG 3' (SEQ ID No. 5); and
5'TACGTGCGGACAGGGCCTGA 3' (SEQ ID No. 4).
11. A method according to any preceding claim further comprising the step of analysing the amplification product by restriction digestion and size analysis.
12. A method according to any preceding claim wherein the disease or disorder is ischaemic heart disease.
13. A method according to any one of claims 1 – 11 wherein the disease or disorder is Nephrotic Syndrome.
14. A method according to any one of claims 1 – 11 wherein the disease or disorder is an inflammatory joint disorder.
15. A method according to claim 14 wherein the disorder is Rheumatoid Arthritis.
16. A method according to any one of claims 1 – 11 wherein the disease or disorder is cancer.

R.A.34
19-09-2001

FILE No.899 19.09.'01 15:08

ID:MARKS & CLERK (LEEDS)

3.0002023.0 .052002
GB000243C

FAX:0113 389 5601

PAGE 6

46

17. A method according to claim 16 wherein the cancer is Ovarian Carcinoma
18. A method according to any one of claims 1 – 11 wherein the disease or disorder is diabetes, or complications thereof, or proteinuria.